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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,332	04/06/2007	David W. Morris	PP023362.0003	5041

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
08/23/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,332	MORRIS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 37-55* is/are pending in the application.

4a) Of the above claim(s) *1-32 and 37-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/03/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments and Amendments

1. Claims 1-34 and 37-55 are pending.

Claims 35 and 36 have been cancelled.

Claims 1-32 and 37-55, drawn to non-elected inventions are not examined on the merits.

Claims 33 and 34 have been amended.

Claims 33 and 34 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claims 35 and 36 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants' cancellation of the claims.

New and Maintained Rejections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 33 and 34 are broadly drawn to kits comprising methods of detecting at least two target polynucleotides within a test sample that selectively hybridize with two CA polynucleotide sequences that share at least 95% identity with sequences listed in the claims, its complements or fragments indicative of cancer. Although the claims do not explicit note one of ordinary skill in the art can readily assume the assays implemented are molecular-based techniques.

The specification does not enable one of ordinary skill in the art to definitively assess the incidence of any type of cancer with complements and fragments of any of the sequences listed in claims 33 and 34. There is no disclosure designating what changes to the coding sequences could be

tolerated enabling one of ordinary skill in the art to make and use the said sequences in any diagnostic method. The experimental design presented in the specification lacks information regarding the applicability of variants, mutants, degenerate coding sequences thereof and sequences sharing less than 100% sequence identity to the wild type sequences in diagnostic methods relative to cancer. Given the differing pathologies of cancer it is not reasonable to conclude that each of the sequences and their degenerate coding sequences would be effective in yielding a discriminate diagnosis between distinct cancers.

Applicants have not set forth any supporting evidence that suggests that fragments and complements of any of the sequences listed in the claims are unique tumor or molecular markers for cancer in general. In addition, the molecular-based techniques presented in the specification do not take into account the possibility that results from such diagnostic tests can be obscured by the presence of excess normal DNA. It is art known that molecular-based assays are valid tools used in predicting and detecting diseases, however as assessed in a review authored by Tascilar et al. (Annals of Oncology 10,Suppl. 4:S107-S110, 1999) "...these tests should be interpreted with caution..." and "the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated prudently".

Furthermore, Tockman et al. (Cancer Research 52:2711s-2718s, 1992)

teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders. Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. "This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]", see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers,

markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder is highly speculative and unpredictable.

Based on the analysis and the teachings presented above it would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification for the enablement of the broadly claimed invention. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 33 and 34 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. It is not clear if the "95% identity" referenced in the claims is for example, sequence identity and/or functional identity. Applicants should further clarify the claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**
>
> **(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.**
>
> **(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.**

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. The rejection of claim 33 under 35 U.S.C. 102(e) as being anticipated by Knoll et al./ U.S. Patent number 7,014,997 B2 (filed May 14, 2001) is maintained. Claim 35 has been cancelled.

Applicants assert the amendment to claim 33 obviates the instant rejection and furthermore the alignment provided by the Office in the Action mailed March 3, 2010 shows only 65.9 percent and 36.8 percent identity to Applicants' SEQ ID NOS: 4 and 427, respectively, see Remarks submitted June 3, 2010, page 16, last paragraph. The amendment and Applicants' points of view have been carefully considered, but found unpersuasive.

Claim 33 includes "at least 95% identity" and "complements", whereas a kit comprises at least two polynucleotides that selectively hybridize with at least 95% identity to at least two CA polynucleotide sequences or its complements. Applicants' specification does not seem to adequately define the term, complements. The specification on page 41 seems to suggest complements may be 8-12 nucleotides or longer, "complementarity need not be perfect" and does not need to be a *full* complement. In the absence of a definitive description of the term, complement the prior art reads on the claim and the limited sequence homology language now of record in the claim the rejection is maintained and reiterated below.

Knoll discloses sequences that would selectively hybridize to Applicants' SEQ ID NO: 4 and SEQ ID NO: 427 or their complements within in a sample, see sequence alignment information of record in the action mailed March 3, 2010; column 1, lines 36-45; and column 14, lines 56-65. Knoll discloses sequences 425 and 148, which are the same as Applicants' SEQ ID NO: 4 and SEQ ID NO: 427, respectively, corresponding hybridization probes, arrays, and kits in which these components are contained, see abstract; column 2, lines 5-50; column 3, lines 17-25; bridging paragraph of columns 24 and 25; and the claims beginning in column 37. These components are useful in detecting "[c]hromosomal abnormalities often common and ...diagnostic in...leukemia and other cancers", see column 2, 1st full sentence.

10. The rejection of claim 33 under 35 U.S.C. 102(e) as being anticipated by Cargill et al./ U.S. Patent Application Publication number 2005/0026169 A1 (effective filing date April 30, 2003) is maintained. Claim 35 has been cancelled.

Applicants assert the amendment to claim 33 obviates the instant rejection and furthermore the alignment provided by the Office in the Action mailed March 3, 2010 shows only 73 percent and 17.7 percent identity to Applicants' SEQ ID NOS: 4 and 427, respectively, see Remarks submitted June 3, 2010, page 17, 2nd paragraph. The amendment and

Applicants' points of view have been carefully considered, but found unpersuasive.

Claim 33 includes "at least 95% identity" and "complements", whereas a kit comprises at least two polynucleotides that selectively hybridize with at least 95% identity to at least two CA polynucleotide sequences or its complements. Applicants' specification does not appear to adequately define the term, complements. The specification on page 41 seems to suggest complements may be 8-12 nucleotides or longer, "complementarity need not be perfect" and does not need to be a *full* complement. In the absence of a definitive description of the term, complement the prior art reads on the claim and the limited sequence homology language now of record in the claim the rejection is maintained and reiterated below.

Cargill discloses sequences that would selectively hybridize to Applicants' SEQ ID NO: 4 and SEQ ID NO: 427 or their complements within in a sample, see sequence alignment information of record in the action mailed March 3, 2010; page 3, sections 0023 and 0024; and page 14, section 0153. Cargill discloses sequences 17996 and 17977, which are the same as Applicants' SEQ ID NO: 4 and SEQ ID NO: 427, respectively, corresponding hybridization probes, arrays, DNA chips and kits in which these components are contained, see abstract; page 14, sections 0154 and 0155; page 15, section 0162; and page 16, section 0173-page 18, section 0186.

11. The rejection of claim 34 under 35 U.S.C. 102(e) as being anticipated by Venter et al./ U.S. Patent number 6,812,339 B1 (filed September 10, 2001) is maintained. Claim 36 has been cancelled.

Applicants assert the amendment to claim 34 obviates the instant rejection and furthermore the alignment provided by the Office in the Action mailed March 3, 2010 shows only 32.2 percent to Applicants' SEQ ID NOS: 622, see Remarks submitted June 3, 2010, page 17, 2nd paragraph. Furthermore, Applicants aver Venter's sequence 340 does not share at least 95% identity to Applicants' SEQ ID NO: 53. Applicants also note Venter does not imply or disclose any association between the disclosed SNPs and cancer, see sentence bridging pages 17 and 18 of the Remarks. The amendment and Applicants' points of view have been carefully considered, but found unpersuasive.

Claim 34 includes "at least 95 identity" and "complements", whereas a kit comprises at least two polynucleotides that selectively hybridize with at least 95% identity to at least two CA polynucleotide sequences, fragments thereof or its complement. The sequences disclosed by Venter read on fragments, as well as complements. Applicants' specification does not appear to adequately define the term, complements. The specification on page 41 seems to suggest complements may be 8-12 nucleotides or longer, "complementarity need not be perfect" and does not need to be a

full complement. In the absence of a definitive description of the term, complement the prior art reads on the claim and the limited sequence homology language now of record in the claim the rejection is maintained and reiterated below.

Venter discloses sequences that would selectively hybridize to Applicants' SEQ ID NO: 53 and SEQ ID NO: 622, fragments thereof or their complements within in a sample, see sequence alignment information following instant rejection; column 5, lines 32-47; and column 18, lines 24-63. Venter discloses sequences 340 and 3171, which are the same as Applicants' SEQ ID NO: 53 and SEQ ID NO: 622, respectively, corresponding hybridization probes and kits in which these components are contained, see column 14, lines 39-54; and columns 15 and 16.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the

THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a *flexible schedule*, however she can normally be reached Monday through Saturday, 7:30 am to 6:30 pm with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
04 August 2010
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643